

IPEA/EP

## **PCT**

**CHAPTER II** 

#### **DEMAND**

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only				
Identification of IPEA		Date of receipt of DEMAND		
Box No. I IDENTIFICATION OF T	HE INTERNATIONAL	APPLICATION	Applicant's or agent's file reference GI-003 PCT	
International application No.	International filing date	(day/month'year)	(Earliest) Priority date (day/month/year)	
PCT/EP00/09130	18 September 2000	0 (18/09/2000)	16 September 1999 (16/09/1999)	
Title of invention	1			
A New Assay to Detect Substance	es Useful for the The	rapy of Cancer an	d Infectious Diseases	
Box No. II APPLICANT(S)				
Name and address: (Family name followed by The address must include p	given name; for a legal entity; ostal code and name of country.	full official designation. )	Telephone No.:	
Max-Planck-Gesellschaft zur Förd Hofgartenstrasse 8 80539 München	erung der Wissensch	naften e.V.	Facsimile No.:	
Germany			Teleprinter No.:	
State (that is, country) of nationality:		State (that is, count	ry) of residence:	
DE		DE		
Name and address: (Family name followed by §	given name; for a legal entity, fi	ill official designation. The	address must include postal code and name of country.)	
NIELSEN, Erik Im Schutzenecker 9 69181 Leimen				
Germany				
State (that is, country) of nationality: US		State (that is, count	yy) of residence	
Name and address: (Family name followed by given name; for a legal entity, fill official designation. The address must include postal code and name of country)				
CHRISTOPHORIDIS, Savvas Boxbergring 107 69126 Heidelberg Germany				
State (that is, country) of nationality:  State (that is, country) of residence				
State (that is, country) of nationality:  GR		DE	of residence.	
Further applicants are indicated on	Further applicants are indicated on a continuation sheet.			

International application No. PCT/EP00/09130

Continuation of Box No. II APPLICANT(S)			
If none of the following sub-boxes is used, this sheet should not be included in the demand.			
Name and address: (Family name followed by given name: for a legal entity, f MURPHY, Carol Alexandrou Papenastasiou 4 45 500 Anatoli, Ioannina Greece	full official designation. The address must include postal code and name of country)		
State (that is, country) of nationality:  IE	State (that is, country) of residence:  GR		
Name and address: (Family name followed by given name; for a legal entity, fill official designation. The address must include postal code and name of country.)  ZERIAL, Marino Heuauerweg 30/1 69124 Heidelberg Germany			
State (that is, country) of nationality:	State (that is, country) of residence:  DE		
Name and address: (Family name followed by given name, for a legal entity, field official designation. The address must include postal code and name of country.)  DE RENZIS, Stefano Meyerhofstrasse 1 69117 Heidelberg Germany			
State (that is, country) of nationality:	State (that is, country) of residence.  DE		
Name and address: (Family name followed by given name, for a legal entity, fi	State (that is, country) of residence:		
Further applicants are indicated on another continuation sho	eet.		

International application No. PCT/EP00/09130

	l		
Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CO	RRESPONDENCE		
The following person is  agent  common representative			
and has been appointed earlier and represents the applicant(s) also for international pre	liminary examination.		
is hereby appointed and any earlier appointment of (an) agent(s)/common represer	stative is hereby revoked.		
is hereby appointed, specifically for the procedure before the International Prelimi the agent(s)/common representative appointed earlier.	nary Examining Authority, in addition to		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)	Telephone No.:		
DEHMEL, Albrecht	0049-(0)89-238852-6		
DEHMEL & BETTENHAUSEN	Facsimile No.:		
Patentanwälte Müllerstr. 1	0049-(0)89-238852-70		
80469 München			
Germany	Teleprinter No.:		
Address for correspondence: Mark this check-box where no agent or common respace above is used instead to indicate a special addr ess to which correspondence	epresentative is/has been appointed and the should be sent.		
Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION			
Statement concerning amendments:*  1. The applicant wishes the international preliminary examination to start on the basis of:  the international application as originally filed the description as originally filed as amended under Article 3-4			
the claims  as originally filed  as amended under Article 19 (together with any accompanying as amended under Article 34	statement)		
the drawings as originally filed as amended under Article 34			
2. The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.			
3. The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). (This checkbox may be marked only where the time limit under Article 19 has not yet expired.)			
* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.			
Language for the purposes of international preliminary examination: English			
which is the language in which the international application was filed.			
which is the language of a translation furnished for the purposes of international search.			
which is the language of publication of the international application.			
which is the language of the translation (to be) furnished for the purposes of international preliminary examination.			
Box No. V ELECTION OF STATES			
The applicant hereby elects all eligible States (that is, all States which have been designat the PCT)	ed and which are bound by Chapter II of		
excluding the following States which the applicant wishes not to elect:			

International application No. PCT/EP00/09130

Box No. VI CHECK LIST					
The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:  For International Preliminary  Examining Authority use only					
translation of international application	:	sheets	received	not received	
2 amendments under Article 34	,	sheets			
	•	Sheets			
copy (or, where required, translation) of amendments under Article 19	:	sheets			
copy (or, where required, translation) of statement under Article 19	:	sheets			
5. letter	:	sheets			
6. other (specify)	:	sheets			
The demand is also accompanied by the item(s) m	arked below:				
1. 🗶 fee calculation sheet		4. statement ex	plaining lack of sign.	ature	
2. separate signed power of attorney		5. nucleotide ar computer rea	nd or amino acid seq	uence listing in	
3. copy of general power of attorney; reference number, if any:		6. other (specify			
Box No. VII SIGNATURE OF APPLICANT, A	AGENT OR CO	MMON REPRESEN	TATIVE		
Next to each signature, indicate the name of the person signing				rom reading the demand).	
Munich, 6 April 2001 Dr. Albrecht Dehmel					
, Wallon, 6 / Phi 2001		pean Patent Attorn	еу		
For Internatio	onal Preliminary Ex	camining Authority us	e only —		
Date of actual receipt of DEMAND:					
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):					
The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.  The applicant has been informed accordingly.					
The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.					
Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.					
For International Bureau use only					
Demand received from IPEA on:					

## **PCT**

## REQUEST

For receiving Office use only
International Application No
International Filing Date
Name of receiving Office and "PCT International Application"

REQUEST	International Filing Date	
The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.	Name of receiving Office and "PCT International Application"	
according to the Patent Cooperation 17649	Applicant's or agent's file reference (if desired) (12 characters maximum) GI-003 PCT	
Box No. I TITLE OF INVENTION		
	acracy of Cancer and Infectious Diseases	
A New Assay to Detect Substances Useful for the Tr	lerapy of Cancer and Infections Diseases	
Box No. II APPLICANT		
Name and address: (Family name followed by given name; for a designation. The address must include postal code and name of coaddress indicated in this Box is the applicant's State (that is, count of residence is indicated below.)	a legal entity, full official ountry. The country of the try) of residence if no State	
	Telephone No.	
Max-Planck-Gesellschaft zur Förderung der Wissens Hofgartenstrasse 8 80539 München	Facsimile No.	
	Teleprinter No.	
State (that is, cowing) of nationality:  DE	State (that is, country) of residence: DE	
This recon is applicant all designated [ all designated ]	ated States except the United States of America only the States indicated in the Supplemental Box	
Box No. III FURTHER APPLICANT(S) AND/OR (FUR	THER) INVENTOR(S)	
Name and address: (Family name followed by given name; for designation. The address must include postal code and name of a address indicated in this Box is the applicant's State (that is, coun of residence is indicated below)  NIELSEN, Erik Im Schutzenecker 9 69181 Leimen	a legal entity, fill official country. The country of the hoty) of residence if no State  This person is:  applicant only  applicant and inventor  inventor only (If this check-box is marked, do not fill in below.)	
State (that is, country) of nationality: US	State (that is, country) of residence: DE	
This person is applicant all designated all design	nated States except of America the United States of the States indicated in the Supplemental Box	
Further applicants and or (further) inventors are indicate	ed on a continuation sheet.	
Box No. IV AGENT OR COMMON REPRESENTATI	VE; OR ADDRESS FOR CORRESPONDENCE	
The person identified below is hereby has been appointed to a of the applicant(s) before the competent International Authori	ties as.	
Name and address: (Family name followed by given name:	or a legal entity, full official   Telephone No. al code and name of country.)   0049-(0)89-238852-6	
DEHMEL, Albrecht	Facsimile No	
Dehmel & Bettenhausen	0049-(0)89-238852-70	
Müllerstrasse 1 80469 München	Teleprinter No.	
OUTOS Manores		
	the second or common representative is his been appointed and the	
Address for correspondence: Mark this check-box wh space above is used instead to indicate a special address	ere no agent or common representative is has been appointed and the to which correspondence should be sent.  See Notes to the request for	

Continuation of Box No. III FURTHER APPLICANT(S) A	ND/OR (FURTHER) INVENTOR(S)			
If none of the following sub-boxes is used, this sheet should not be included in the request.				
Name and address. (Family name followed by given name: for a l designation. The address must include postal code and name of coun address indicated in this Box is the applicant's. State (that is, country, of residence is indicated below.)  CHRISTOPHORIDIS, Savvas  Boxbergring 107 69126 Heidelberg	ntry. The country of the			
State (that is, country) of nationality: GR	State (that is, country) of residence: DE			
This person is applicant all designated for the purposes of:  all designated the United States	States except the United States the States indicated in the Supplemental Box			
Name and address: (Family name followed by given name: for a lad designation. The address must include postal code and name of could address indicated in this Box is the applicant's State (that is, country, of residence is indicated below.)  MURPHY, Carol Alexandrou Papenastasiou 4 45 500 Anatoli, Ioannina	This person is:  The country of the position o			
State (that is, country) of nationality:	State (that is, country) of residence: GR			
This person is applicant all designated for the purposes of:	States except the United States the States indicated in the Supplemental Box			
Name and address: (Family name followed by given name, for a designation. The address must include postal code and name of counting address indicated in this Box is the applicant's State (that is, country of residence is indicated below.)  ZERIAL, Marino  Heuauerweg 30/1 69124 Heidelberg	norv i ne country of the			
State (that is, country) of nationality:	State (that is, country) of residence: DE			
This person is applicant all designated for the purposes of:  all designated the United States	d States except ates of America only the States indicated in the Supplemental Box			
Name and address: (Family name followed by given name; for a designation. The address must include postal code and name of country address indicated in this Box is the applicant's State (that is, country of residence is indicated below)  DE RENZIS, Stefano  Meyerhofstrasse 1 69117 Heidelberg	mirv. The country of the			
State (that is, country) of nationality:	State (that is, country) of residence DE			
	d States except tates of America only the States indicated in the Supplemental Box			
Further applicants and or (further) inventors are indicated on another continuation shee:				

Box N					
	llowing designations are hereby made under Rule 4.9(a) (m	ark the a	oplicable check-boxes; at least one must be marked):		
Region	nal Patent				
_	ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, MZ Mozambique, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT				
	A Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT				
<b>☑</b> EF	European Patent: AT Austria, BE Belgium, CH at DK Denmark, ES Spain, FI Finland, FR France, GB Um MC Monaco, NL Netherlands, PT Portugal, SE Sweden, a	rited Ku	witzerland and Liechtenstein, CY Cyprus, DE Germany, ngdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, other State which is a Contracting State of the European Patent		
□ O.	Convention and of the PCT  OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)				
Natio	nal Patent (if other kind of protection or treatment desired, spec				
☐ AI	United Arab Emirates	ПLC	Saint Lucia		
☐ A(	Antigua and Barbuda	=	Sri Lanka		
	Albania	LR	Liberia		
-	I Armenia	□ LS	Lesotho		
A1	Austria		Lithuania		
	J Australia	LU	Luxembourg		
_	Z Azerbaijan	_	Latvia		
☐ B.	Bosnia and Herzegovina	☐ M.4	Morocco		
	Barbados		Republic of Moldova		
□во	Bulgaria		Madagascar		
	R Brazil	☐ MH	The former Yugoslav Republic of Macedonia		
	Belarus	$\square$ MN	i Mongolia		
⊟ ва	Z Belize	□ M\	V Malawi		
<b>☑</b> C.	A Canada		Mexico		
□ C1	H and LI Switzerland and Liechtenstein	□ M2	Z Mozambique		
□ c	N China	□ NO	Norway		
□ c	R Costa Rica	□ NZ	New Zealand		
□ C	U Cuba	□ PL	Poland		
□ c:	Z Czech Republic	□РТ	Portugal		
□ D:	E Germany	☐ RC			
	K Denmark	☐ RU	Russian Federation		
	M Dominica	□ SD	Sudan		
	Z Algeria	☐ SE	Sweden		
□ E	E Estonia	□ sc			
☐ E:	S Spain	☐ SI	Slovenia		
☐ F	Finland	☐ SK			
□ G	B United Kingdom		Sierra Leone		
	D Grenada	□ TJ	Tajikistan		
	E Georgia	□ TN			
□ G	H Ghana	☐ TF			
	M Gambia	□ тт	· ·		
	R Croatia	☐ T2	•		
□н	U Hungary	U UA			
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	I India	∐ UZ			
□ J		∐ Yī	· ·		
	E Kenya	$\bigcup Z_i$			
□ к	G Kyrgyzstan		V Zimbabwe		
□ K	P Democratic People's Republic of Korea	Check	-box reserved for designating States which have become the PCT after issuance of this sheet:		
□к	KR Republic of Korea				
□ к	Z Kazakhstan	Ц.			
Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)					

Box No. VI PRIORITY CLAIM Further priority claims are indicated in the Supplemental Box						
Filing date	Number of earlier application		Where earlier application is:			
of earlier application (day/month year)	of earner applicatio	national application: country	regional application:* regional Office	international application receiving Office		
item (1) 16 September 1999 (16/9/1999)	99 118 385.6	EP				
item (2)						
item (3)						
The receiving Office is recoff the earlier application( purposes of the present in	s) (only if the eartier a,	ransmit to the International B pplication was filed with the is the receiving Office) identi	Office which for the			
<ul> <li>Where the earlier application is Convention for the Protection of Ir</li> </ul>	ndustrial Property for white	ch that earlier application was fi	Supplemental Box at least on led (Rule 4.10(b)(u)). See Si	e country party to the Parts upplemental Box.		
Box No. VII INTERNATIO	ONAL SEARCHING	AUTHORITY				
Choice of International Searc (if two or more International Se competent to carry out the intern the Authority chosen; the two-letter	arching Authorities are lational search, indicate	Request to use results of essearch has been carried out by a Date (day/month year)	or requested from the Interna-	to that search (if an earlier tional Searching Authority):  Country (or regional Office)		
ISA/ EP	toue muy be used).	28/02/2000	99 118 385.6	EP .		
Box No. VIII CHECK LIST	T; LANGUAGE OF I	FILING				
This international application of the following number of shee	ts:	itional application is accompa	nnied by the item(s) mark	ed below:		
request : 4	1. Li lee c	alculation sheet				
description (excluding sequence listing part) : 35		rate signed power of attorney of general power of attorney		.y:		
claims : 3	<del></del>	ment explaining lack of signa				
abstract : 1						
drawings		6. I translation of international application into (language):				
sequence listing part						
of description : 34	8. 🗗 nucle	8. nucleotide and or amino acid sequence listing in computer readable form				
Total number of sheets: 77 9.  other (specify): Receipt for documents; crossed cheque						
Figure of the drawings which should accompany the abstract:  Language of filing of the international application:  English						
	OF APPLICANT OF					
Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).						
Munich, September 18, 2000 pr. Albrecht Dehmel D-80469 München						
	1	For receiving Office use only				
Date of actual receipt of the international application:	ne purported			2. Drawings:		
Corrected date of actual re timely received papers or of the purported international	drawings completing			received.		
4. Date of timely receipt of the corrections under PCT Ar	ticle 11(2).			not received.		
5. International Searching Au (if two or more are competed)	uthority tent): ISA/		ittal of search copy delaye arch fee is paid.	ed		
	For	International Bureau use on	ly			
Date of receipt of the record	copy					

From the: INTERNATIONAL PRELIMINARY EX	AMINING AUTHORITY				
То:	Frist: 22. M VF:	22. 10.19	DCT		
DEHMEL, Albrecht		22.70.	PCI		
DEHMEL & BETTENHAUSEN Müllerstrasse 1 D-80469 München	Eingegangen 24. Aug. 2	001	WRITTEN OPINION		
ALLEMAGNE	DEHMEL & BETT Patentan w	i	(PCT Rule 66)		
		Date of mailing (day/month/year)	22.08.2001		
Applicant's or agent's file reference GI-003 PCT		REPLY DUE	within 3 month(s) from the above date of mailing		
International application No. PCT/EP00/09130	International filing date (c	day/month/year)	Priority date (day/month/year) 16/09/1999		
International Patent Classification (IPC)	or both national classification an	d IPC	J		
C12Q1/44					
Applicant					
MAX-PLANCK-GESELLSCHAI	FT ZUR FÖRDERUNG DE	R			
This written opinion is the first	t drawn up by this Internation	al Preliminary Exami	ining Authority		
·		•	rining ruthorny.		
2. This opinion contains indication	ons relating to the following ite	ems:			
I 🗵 Basis of the opinion					
II Priority					
III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability					
	,				
	ent under Rule 66.2(a)(ii) with anations supporting such stat		nventive step or industrial applicability;		
VI Certain document cited					
VII 🗀 Certain defects in	the international application				
VIII 🖾 Certain observatio	ons on the international applic	ation			
3. The applicant is hereby <b>invite</b>	d to reply to this opinion.				
	licated above. The applicant may, y to grant an extension, see Rule		f that time limit,		
	en reply, accompanied, where applanguage of the amendments, se		nts, according to Rule 66.3.		
Also: For an additional opportunity to submit amendments, see Rule 66.4.  For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  For an informal communication with the examiner, see Rule 66.6.					
If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.					
4. The final date by which the international preliminary					
examination report must be established according to Rule 69.2 is: 16/01/2002.					
Name and mailing addrage of the intern		Authorized officer / Ex	aminor		

Name and mailing address of the international preliminary examining authority:



European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465

Wieser, M

Formalities officer (incl. extension of time limits)

Digiusto, M

Telephone No. +49 89 2399 8162





١.	Basis	of	the	opinion
----	-------	----	-----	---------

	Basis of the opinion  With regard to the elements of the international application.  Office in response to an invitation under Article	(Replacement sheets which have been furnished to
١.	Basis of the opinion  With regard to the elements of the international application the receiving Office in response to an invitation under Article	e 14 are referred to in this op-

the receiving Office in re	esponse to any
Description, pages:	
1-69	as originally filed
Claims, No.:	as originally filed
Sequence listing pa	rt of the description, pages:
36-69, as originally fi	led
These elements we	inguage, all the elements marked above were available or furnished to this Authority in the ne international application was filed, unless otherwise indicated under this item.  The available or furnished to this Authority in the following language: , which is:  The atranslation furnished for the purposes of the international search (under Rule 23.1(b)).
the language of the language of the language of 55.2 and/or 55.3. With regard to any international prelim	of a translation of the wood for the purposes of international preliminary oxed of a translation furnished for the purposes of international preliminary oxed 5.3).  I nucleotide and/or amino acid sequence disclosed in the international application, the mucleotide and/or amino acid sequence disclosed in the sequence listing:
<ul> <li>□ contained in</li> <li>□ filed togethe</li> <li>□ furnished su</li> <li>□ turnished su</li> <li>□ The statem the internat</li> <li>□ The statem listing has</li> </ul>	the international application in written form.  r with the international application in computer readable form.  besequently to this Authority in written form.  besequently to this Authority in computer readable form.  besequently to this Authority in computer readable form.  ent that the subsequently furnished written sequence listing does not go beyond the disclosure in ional application as filed has been furnished.  ional application as filed has been furnished.  ient that the information recorded in computer readable form is identical to the written sequence been furnished.
<ol> <li>The amendment</li> <li>the descript</li> <li>the claims</li> </ol>	Nac'

#### WRITTEN OPINION

International application No. PCT/EP00/09130

	the drawings,	sheets:					
5.	This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):						
	(Any replacement sh report.)	eet containing such amendments must be referred to under item 1 and annexed to this					

- 6. Additional observations, if necessary:
- V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- 1. Statement

Novelty (N)

Claims 11

Inventive step (IS)

Claims 12,13

Industrial applicability (IA) Claims

2. Citations and explanations see separate sheet

#### VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made: see separate sheet

#### Section V

Claims 1-10 refer to the use of an effector of a GTPase, preferably of the Rab family, as a target in drug screening in a vast class of diseases.

The only document cited in the International Search Report which is concerned with GTPase effectors is NATURE, vol.397, 1999, pages 621-25 (document A), which does not disclose or even suggest the use of these effectors in drug screening.

Therefore, the subject-matter of claims 1-10 is considered to be novel and inventive within the meaning of Articles 33(2) and 33(3) PCT.

Claim 11 refers to a kit, merely characterised by containing at least one GTPase effector/regulator molecule. Since such effector/regulator molecules are known in the art (see for instance document A), claim 11 is not novel (Article 33(2) PCT).

The scope of claims 12 and 13 encompasses a kit additionally containing a GTPase, preferably of the Rab family. A skilled person when performing the experiments described in document A, is using these two substances. No inventive step is involved in merely packing these well known compounds into a kit of parts. The claims do not meet the requirements of Article 33(3) PCT.

#### Section VIII

The claims are not supported by the description (Article 6 PCT), which does not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a skilled person (Article 5 PCT). The description does not contain any information concerning the usefulness of a substance identified by the screening assay of claims 1-10 as pharmaceutical agent. The assay described in the examples allows only to determine whether or not a substance tested modulates the activity of an GTPase effector.



From the INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: DEHMEL, Albrecht	Frist:	VF:			PCT
DEHMEL & BETTENH	AUSEN Ei <b>ngegange</b> n	2 1. Dez. 2001	i	THE INTER	ON OF TRANSMITTAL OF NATIONAL PRELIMINARY MINATION REPORT
	DEHMEL	& BETTENHA	USEN	(	PCT Rule 71.1)
		Patentanwälte	Date of r	_	18.12.2001
Applicant's or agent's file refe GI-003 PCT	erence			IMPO	ORTANT NOTIFICATION
International application No. PCT/EP00/09130		International filing date (c	lay/month/y	· 1	Priority date <i>(day/month/year)</i> 16/09/1999
Applicant MAX-PLANCK-GESEL	LSCHAFT Z	UR FÖRDERUNG D	ER		

- 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

Authorized officer

European Patent Office D-80298 Munich

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## PATENT COOPERATION TREATY

## PCT

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	REC'D	27 DEC 2001
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		PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's	or age	ent's file reference	T		See Notific	ation of Transmittal of International
GI-003 F	СТ		FOR FURTHER ACT	TION		Examination Report (Form PCT/IPEA/416)
Internation	ai appl	ication No.	International filing date (da	ay/month/	year)	Priority date (day/month/year)
PCT/EP	00/09	130	18/09/2000			16/09/1999
Applicant MAX-PL  1. This i and is	ANCI	A-GESELLSCHAFT Zonational preliminary examismitted to the applicant and PRT consists of a total of a port is also accompanies mended and are the base	according to Article 36.  4 sheets, including this of the ANNEXES, i.e. sheets for this report and/or sometimes of the Administrative in the Administrativ	repared	eet. description	rnational Preliminary Examining Authority  n, claims and/or drawings which have ctifications made before this Authority e PCT).
3. This r II III IV V VI VIII		Basis of the report Priority Non-establishment of o Lack of unity of invention Reasoned statement uncitations and explanation Certain documents cite Certain defects in the in	on nder Article 35(2) with reg ons suporting such staten ed	elty, inve gard to n nent	•	and industrial applicability ntive step or industrial applicability;
Date of sub		n of the demand		Date of co	ompletion of t	his report
	examii Euro D-80 Tel	address of the internationa ning authority: pean Patent Office 298 Munich -49 89 2399 - 0 Tx 523656 +49 89 2399 - 4465		Authorize Wieser,	М	2200 8424

Telephone No. +49 89 2399 8434

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/09130

### I. Basis of the report

1.	the and	receiving Office in r	ents of the international application (Replacement sheets which have been furnished to esponse to an invitation under Article 14 are referred to in this report as "originally filed" this report since they do not contain amendments (Rules 70.16 and 70.17)):
	1-6	9	as originally filed
	Cla	ims, No.:	
	1-1	3	as originally filed
	Sec	quence listing part	of the description, pages:
	36-	69, as originally filed	
2.			uage, all the elements marked above were available or furnished to this Authority in the iternational application was filed, unless otherwise indicated under this item.
	The	ese elements were a	vailable or furnished to this Authority in the following language: , which is:
		the language of a tr	ranslation furnished for the purposes of the international search (under Rule 23.1(b)).
		the language of pub	plication of the international application (under Rule 48.3(b)).
		the language of a tr 55.2 and/or 55.3).	anslation furnished for the purposes of international preliminary examination (under Rule
3.		•	eotide and/or amino acid sequence disclosed in the international application, the examination was carried out on the basis of the sequence listing:
	⊠	contained in the inte	ernational application in written form.
	$\boxtimes$	filed together with the	ne international application in computer readable form.
		furnished subseque	ently to this Authority in written form.
		furnished subseque	ently to this Authority in computer readable form.
			the subsequently furnished written sequence listing does not go beyond the disclosure in plication as filed has been furnished.
		The statement that listing has been furn	the information recorded in computer readable form is identical to the written sequence nished.
4.	The	amendments have i	resulted in the cancellation of:
		the description,	pages:
		the claims,	Nos.:
		the drawings,	sheets:

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/09130

5.	This report has been established as if (some of) the amendments had not been made, since they have been
	considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes:

s: Claims 1-10,12,13

No:

Claims 11

Inventive step (IS)

Yes:

Claims 1-10

No:

Claims 12,13

Industrial applicability (IA)

Yes:

Claims 1-13

No: Claims

2. Citations and explanations see separate sheet

#### VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made: see separate sheet

#### Section V

Claims 1-10 refer to the use of an effector of a GTPase, preferably of the Rab family, as a target in drug screening in a vast class of diseases.

The only document cited in the International Search Report which is concerned with GTPase effectors is NATURE, vol.397, 1999, pages 621-25 (document A), which does not disclose or even suggest the use of these effectors in drug screening.

Therefore, the subject-matter of claims 1-10 is considered to be novel and inventive within the meaning of Articles 33(2) and 33(3) PCT.

Claim 11 refers to a kit, merely characterised by containing at least one GTPase effector/regulator molecule. Since such effector/regulator molecules are known in the art (see for instance document A), claim 11 is not novel (Article 33(2) PCT).

The scope of claims 12 and 13 encompasses a kit additionally containing a GTPase, preferably of the Rab family. A skilled person when performing the experiments described in document A, is using these two substances. No inventive step is involved in merely packing these well known compounds into a kit of parts. The claims do not meet the requirements of Article 33(3) PCT.

#### Section VIII

The claims are not supported by the description (Article 6 PCT), which does not disclose the invention in a manner sufficiently clear and complete for it to be carried out by a skilled person (Article 5 PCT). The description does not contain any information concerning the usefulness of a substance identified by the screening assay of claims 1-10 as pharmaceutical agent. The assay described in the examples allows only to determine whether or not a substance tested modulates the activity of an GTPase effector.

Claims to the use of a substance in an in vivo assay, wherein human beings are not explicitly excluded from the test organisms, could lead to problems in various national jurisdictions.

### CATENT COOPERATION THE ATY

To:

From the	INT	<b>ERNA</b>	TIONAL	<b>BUREAU</b>
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### **PCT**

#### **NOTIFICATION OF ELECTION**

(PCT Rule 61.2)

Commissioner

US Department of Commerce United States Patent and Trademark

Office, PCT

2011 South Clark Place Room

CP2/5C24

Arlington, VA 22202 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)
15 May 2001 (15.05.01)

International application No.

PCT/EP00/09130

International filing date (day/month/year)
18 September 2000 (18.09.00)

Applicant's or agent's file reference

GI-003 PCT

Priority date (day/month/year)

16 September 1999 (16.09.99)

Applicant

NIELSEN, Erik et al

X in the demand file	d with the International Preliminary Examining Authority on:
	06 April 2001 (06.04.01)
in a notice effecti	ng later election filed with the International Bureau on:
The election X wa	ıs
	is not
Rule 32.2(b).	ion of 19 months from the priority date or, where Rule 32 applies, within the time limit under

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

Catherine Massetti

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38



## **PCT**

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference		of Transmittal of International Search Report 20) as well as, where applicable, item 5 below.
GI-003 PCT International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
''		
PCT/EP 00/09130	18/09/2000	16/09/1999
Applicant		
MAX-PLANCK-GESELLSCHAFT Z	UR FÖRDERUNG DER	
This International Search Report has bee according to Article 18. A copy is being tra	n prepared by this International Searching Authansmitted to the International Bureau.	nority and is transmitted to the applicant
This International Search Report consists  It is also accompanied by	of a total of3 sheets. a copy of each prior art document cited in this	report.
Basis of the report		
	international search was carried out on the bases otherwise indicated under this item.	sis of the international application in the
the international search w Authority (Rule 23.1(b)).	ras carried out on the basis of a translation of t	he international application furnished to this
was carried out on the basis of th  Contained in the internation	e sequence listing : onal application in written form.	nternational application, the international search
	ernational application in computer readable form	n.
	o this Authority in written form.	
<u> </u>	o this Authority in computer readble form. osequently furnished written sequence listing d	oes not go beyond the disclosure in the
international application a	is filed has been furnished.	ded notige beyond the dissipation in the
the statement that the info furnished	ormation recorded in computer readable form is	s identical to the written sequence listing has been
2. Certain claims were fou	nd unsearchable (See Box I).	
3. Unity of invention is lac	king (see Box II).	
4. With regard to the <b>title</b> ,		
the text is approved as su	ubmitted by the applicant.	
· —	shed by this Authority to read as follows:	
ASSAY TO DETECT SUBSTA	ANCES USEFUL FOR THERAPY	
5. With regard to the <b>abstract</b> ,	the section of the state of the section and	
the text is approved as su the text has been establis within one month from the	ormitted by the applicant. Shed, according to Rule 38.2(b), by this Authori e date of mailing of this international search rep	ty as it appears in Box III. The applicant may, port, submit comments to this Authority.
6. The figure of the <b>drawings</b> to be pub		
as suggested by the appl		None of the figures.
because the applicant fai		<u>.                                    </u>
	characterizes the invention.	

## **PCT**

## WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT) (51) International Patent Classification 6: WO 98/18942 (11) International Publication Number: **A3** C12N 15/55, 15/86, 5/10, 9/16, C07K (43) International Publication Date: 7 May 1998 (07.05.98) 16/40, C12Q 1/68, A61K 38/46 PCT/US97/18581 (81) Designated States: AT, AU, BR, CA, CH, CN, DE, DK, ES, (21) International Application Number: FI. GB, IL, JP, KR, MX, NO, NZ, RU, SE, SG, US, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian 14 October 1997 (14.10.97) (22) International Filing Date: patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, Cl, (30) Priority Data: CM, GA, GN, ML, MR, NE, SN, TD, TG). US 08/741,411 29 October 1996 (29.10.96) Published (71) Applicant (for all designated States except US): INCYTE With international search report. PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Before the expiration of the time limit for amending the claims Palo Alto, CA 94304 (US). and to be republished in the event of the receipt of amendments. (72) Inventors; and (75) Inventors/Applicants (for US only): BANDMAN, Olga (88) Date of publication of the international search report: [US/US]; 366 Anna Avenue, Mountain View, CA 94043 3 September 1998 (03.09.98) (US). AU-YOUNG, Janice [US/US]; 1419 Kains Avenue, Berkeley, CA 94702 (US). (74) Agent: BILLINGS, Lucy, J.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).

(54) Title: NOVEL HUMAN RAB PROTEINS

#### (57) Abstract

The present invention provides four human Rab and Rab-associated proteins (designated collectively as HRAB) and polynucleotides which identify and encode HRAB. The invention also provides genetically engineered expression vectors and host cells comprising the nucleic acid sequences encoding HRAB and a method for producing HRAB. The invention also provides for use of HRAB and agonists, antibodies, or antagonists specifically binding HRAB, in the prevention and treatment of diseases associated with expression of HRAB. Additionally, the invention provides for the use of antisense molecules to polynucleotides encoding HRAB for the treatment of diseases associated with the expression of HRAB. The invention also provides diagnostic assays which utilize the polynucleotide, or fragments or the complement thereof, and antibodies specifically binding HRAB.

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#### WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT) (51) International Patent Classification 6: WO 98/18942 (11) International Publication Number: C12N 15/55, 15/86, 5/10, 9/16, C07K **A3** (43) International Publication Date: 7 May 1998 (07.05.98) 16/40, C12Q 1/68, A61K 38/46 PCT/US97/18581 (21) International Application Number: (81) Designated States: AT, AU, BR, CA, CH, CN, DE, DK, ES, FI, GB, IL, JP, KR, MX, NO, NZ, RU, SE, SG, US, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian (22) International Filing Date: 14 October 1997 (14.10.97) patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, (30) Priority Data: LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, 08/741,411 29 October 1996 (29.10.96) US CM, GA, GN, ML, MR, NE, SN, TD, TG). (63) Related by Continuation (CON) or Continuation-in-Part Published (CIP) to Earlier Application With international search report. 08/741,411 (CIP) US Before the expiration of the time limit for amending the claims 29 October 1996 (29.10.96) Filed on and to be republished in the event of the receipt of amendments. (71) Applicant (for all designated States except US): INCYTE (88) Date of publication of the international search report: 3 September 1998 (03.09.98) PHARMACEUTICALS, INC. [US/US]; 3174 Porter Drive, Palo Alto, CA 94304 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): BANDMAN, Olga [US/US]; 366 Anna Avenue, Mountain View, CA 94043 (US). AU-YOUNG, Janice [US/US]; 1419 Kains Avenue, Berkeley, CA 94702 (US). (74) Agent: BILLINGS, Lucy, J.; Incyte Pharmaceuticals, Inc., 3174 Porter Drive, Palo Alto, CA 94304 (US).

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#### NAL SEARCH REPORT INTERNA'

al Application No PCT/US 97/18581

CLASSIFICATION OF SUBJECT MATTER PC 6 C12N15/55 C12N15/86 IPC 6 C12N5/10 C12N9/16 C07K16/40 C12Q1/68 A61K38/46 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Flectronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. WILSON D.B., WILSON M.P.: "Identification 1-12,18, Х and subcellular localization of human 19 rab5b, a new member of the ras related superfamily of GTPases" JOURNAL OF CLINICAL INVESTIGATION, vol. 89, 1992, NEW YORK, US, pages 996-1005, XP002057689 see abstract see the whole document CHEN D. ET AL.: "Molecular cloning of two Χ 1-10,12, 18,19 novel rab genes from human melanocytes" GENE.. vol. 174, 26 September 1996, AMSTERDAM pages 129-134, XP002057690 see the whole document -/--Further documents are listed in the continuation of box C. Х Patent family members are listed in annex. ΙXΙ Special categories of cited documents : "I" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the \*A\* document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone filing date "L" document which may throw doubts on priority claim(s) or which is cred to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docu-"O" document referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report 1 6 -07- 1998 5 March 1998 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax. (+31-70) 340-3016

Panzica, G

## INTERNAT 'AL SEARCH REPORT

In al Application No
PCT/US 97/18581

Category °	citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
_		į
X	ZAHRAOUI A ET AL: "THE HUMAN RAB GENES ENCODE A FAMILY OF GTP-BINDING PROTEINS RELATED TO YEAST YPT1 AND SEC4 PRODUCTS INVOLVED IN SECRETION" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 264, no. 21, 25 July 1989, pages 12394-12401, XP002015899 see the whole document	1-10,18,
X	EMBL Database, Heidelberg, DE AC: Q13636 "Low MR GTP-binding protein RAB31" Homo Sapiens Author: Bao X. et al. 01-10-96. XP002057691 see abstract	1-12
X	EMBL DataBase, Heidelberg, DE AC:N75242 "yz73g12.rl Homo sapiens cDNA clone 288742 5' similar to PIR:S40208 rab22 protein - dog. EST Author: Hillier L. et al. 05-04-1996 XP002057692 see abstract	1-7,18, 19
Α	WO 89 02898 A (US ARMY) 6 April 1989	12-14
A	LUETCKE A ET AL: "CLONING AND SUBCELLULAR LOCALIZATION OF NOVEL RAB PROTEINS REVEALS POLARIZED AND CELL TYPE-SPECIFIC EXPRESSION"  JOURNAL OF CELL SCIENCE, vol. 107, no. PART 12, December 1994, pages 3437-3448, XP000604112	

## INTERNATIONAL SEARCH REPORT

Ir ational application No.

PCT/US 97/18581

Box I	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This Inter	rnational Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
	Claims Nos: because they relate to subject matter not required to be searched by this Authority, namely:  Remark: Although claim(s) 15-17  is(are) directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
	Claims Nos: because they relate to parts of the international Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3	Claims Nos . because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This Inter	rnational Searching Authority found multiple inventions in this international application, as follows:  See annex
1.	As all required additional search fees were timely paid by the applicant, this international Search Report covers all searchable claims.
2.	As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.	As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4 X	No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-19
Remark	on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

1. Claims: 1-19

An isolated and purified human Rab A (HRABA) protein comprising the aminoacid sequence of Seq. Id. No. 1 or fragments thereof, a nucleic acid sequence encoding for it, comprising Seq. Id. No. 2 or variants thereof; probes, vectors, hosts, production methods thereof, antibodies, agonists and antagonists, their uses, and therapeutic methods therewith.

2. Claims: 20-28

Idem as Subject 1 but limited to human Rab B (hRabB, Seq.Id.Nos. 3 and 4)

3. Claims: 39-57

Idem as Subject 1 but limited to human Rab C (hRabC, Seq.Id.Nos. 5 and 6)

4. Claims: 58-76

Idem as Subject 1 but limited to human Rab D (hRabD, Seq.Id.Nos. 7 and 8)

### INTERNA ONAL SEARCH REPORT

Information on patent family members

PCT/US 97/18581

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 8902898 A	06-04-89	US 4870161 A	26-09-89
		AU 2541488 A	18-04-89
		EP 0393067 A	24-10-90
		JP 2504032 T	22-11-90
		US 5436320 A	25-07-95
		US 5428134 A	27-06-95

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12Q1/44

According to International Patent Classification (IPC) or to both national classification and IPC

#### B. FIELDS SEARCHED

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMI	ENTS CONSIDERED TO BE RELEVANT	
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 42839 A (INCYTE PHARMA INC ;GUEGLER KARL J (US); HILLMAN JENNIFER L (US)) 1 October 1998 (1998-10-01) the whole document	1-13
X	WO 98 18942 A (INCYTE PHARMA INC ;AU YOUNG JANICE (US); BANDMAN OLGA (US)) 7 May 1998 (1998-05-07) the whole document	1-13
X	WO 97 00955 A (INCYTE PHARMA INC) 9 January 1997 (1997-01-09) the whole document	1-13
X	EP 0 856 583 A (WADA MANABU ; JAPAN SCIENCE AND TECHNOLOGY C (JP)) 5 August 1998 (1998-08-05) the whole document 	1-13

X Further documents are listed in the continuation of box C.	Patent family members are listed in annex.
Special categories of cited documents:      'A' document defining the general state of the art which is not considered to be of particular relevance      'E' earlier document but published on or after the international filling date      'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)      'O' document referring to an oral disclosure, use, exhibition or other means      'P' document published prior to the international filling date but later than the priority date claimed	<ul> <li>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</li> <li>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</li> <li>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</li> <li>"&amp;" document member of the same patent family</li> </ul>
Date of the actual completion of the international search  20 November 2000	Date of mailing of the international search report $04/12/2000$
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax: (+31-70) 340-3016	Authorized officer Pellegrini, P

## INTERNATIONAL SEARCH REPORT

PCT/EP 00/09130

Category "	ation) DOCUMENTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Jalegory "	Original of document, with indication, where appropriate, or the relevant passages	
(	CHRISTOFORIDIS S. ET AL.: "The Rab5 effector EEA1 is a core component of endosome docking" NATURE, vol. 397, 18 February 1999 (1999-02-18), pages 621-625, XP002153257 cited in the application the whole document	1-13

## INTERNATIONAL SEARCH REPORT

mation on patent family members

ernational Application No
PCT/EP 00/09130

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
WO 9842839	Α	01-10-1998	US AU US	5843717 A 6774198 A 6010859 A	01-12-1998 20-10-1998 04-01-2000
WO 9818942	Α	07-05-1998	US AU	6124116 A 4903397 A	26-09-2000 22-05-1998
WO 9700955	Α	09-01-1997	AU CA EP	6337596 A 2224247 A 0833908 A	22-01-1997 09-01-1997 08-04-1998
EP 0856583	Α	05-08-1998	JP	10210971 A	11-08-1998